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EXAMINER				
STEELE, AMBER D				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/673,000

Applicant(s)

ROBINSON ET AL.

Examiner

AMBER D. STEELE

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 13-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03/03/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/06)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____
- Page No(s)/Mail Date _____

DETAILED ACTION

Status of the Claims

1. The amendment to the claims received on November 2, 2006 amended claims 3, 5, 8, 11, 14, and 17.

The amendment to the claims received on October 12, 2007 amended claims 1 and 7 and added new claims 19-20.

The amendment to the claims received on March 25, 2008 amended claims 1 and 7 and canceled claims 19-20.

The amendments to the claims received on August 5, 2008 and October 14, 2008 changed the status identifiers only.

Claims 1-18 are currently pending.

Claims 1-12 are currently under consideration.

Election/Restrictions

2. Claims 1-6 are linking claims. Applicants elected Group I (Claims 7-12) in the reply filed on March 28, 2006 without traverse. Thus, claims 13-18 are withdrawn from consideration as being drawn to a nonelected invention.

Priority

3. The present application claims status as a divisional of 09/695,762 filed October 25, 2000, which claims benefit to provisional application 60/161,035 filed October 25, 1999.

Invention as Claimed

4. A method for recovering native protein from a sample comprising protein aggregates, said method comprising the steps of: (a) obtaining a sample comprising protein aggregates

wherein the sample is substantially free of a denaturing agent; (b) subjecting the sample of step (a) to elevated hydrostatic pressure, whereby a portion of protein dissociates from said protein aggregates; c) returning the sample of step (b) to ambient pressure without repeatedly cycling the sample between the elevated and the ambient pressures, whereby a portion of the dissociated protein refolds to native protein and variations thereof.

Withdrawn Rejections

5. The rejection of claims 1-12 under 35 U.S.C. 103(a) as being unpatentable over Litt et al. U.S. Patent 6,635,469 (effective filing date of July 2, 1996) and Silva et al. Anomalous Pressure Dissociation of Large Protein Aggregates The Journal of Biological Chemistry 264(27): 15863-15868, 1989 is withdrawn in view of applicants persuasive arguments.

New Rejections

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. The specification defines "protein aggregate" as "not intended to include the normal association between subunits of a native multi-subunit protein complex or the normal association of capsomeres in a native viral particle" (see page 7, lines 9-12). However, claim 7 requires "said protein aggregates are comprised of protein folding intermediates of a native protein" (see method step (a), lines 2-3). Therefore, in a multi-subunit protein complex the

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intermediates could be subunits. Thus, it is not clear if the claims limit the protein to only monomers or if dimers, trimers, etc. are also included. If dimers, trimers, etc. are also included, then are subunits intermediates? Since, independent claim 7 is a species of independent claim 1 the contradictory definitions of protein aggregates is indefinite for both the genus and species. Furthermore, is the complex utilized in the definition pertaining only to units of different proteins (e.g. ligand-receptor complex, etc.) or to subunits of the same protein (e.g. dimer complex, etc.)?

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 3, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Silva et al. *Anomalous Pressure Dissociation of Large Protein Aggregates* The Journal of Biological Chemistry 264(27): 15863-15868, 1989.

For present claims 1, 3, 7 and 8, Silva et al. teach methods of recovering native protein from a sample comprising protein aggregates comprising (a) obtaining a sample comprising protein aggregates which is free of denaturing agent, (b) subjecting the sample to elevated hydrostatic pressure causing dissociation, and (c) returning the sample to ambient pressure without repeated cycles (please refer to the entire reference particularly the abstract; pages 15863, 15865, 15866; Figures 2-3 and 6-9). Please note: Silva et al. teaches multi-subunit proteins (see the 35 USC 112, second paragraph rejection above).

Therefore, the presently claimed invention is anticipated by the teachings of Silva et al.

10. Claims 1, 3, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonafe et al., 1994, Intermediate States of Assembly in the Dissociation of Gastropod Hemocyanin by Hydrostatic Pressure, Biochemistry, 33: 2651-2660.

For present claims 1, 3, 7, and 8, Bonafe et al. teach methods of pressure-induced aggregate dissociation and refolding of hemocyanin comprising (a) obtaining a sample comprising protein aggregates (i.e. without denaturing agents; protein folding intermediates), (b) subjecting the sample to high pressure wherein a portion dissociates (i.e. not completely dissociated, dimers present), and (c) returning the sample to ambient pressure wherein a portion refolds (please refer to the entire references particularly the abstract; Results section).

Therefore, the presently claimed invention is anticipated by the teachings of Bonafe et al.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonafe et al., 1994, Intermediate States of Assembly in the Dissociation of Gastropod Hemocyanin by

Hydrostatic Pressure, Biochemistry, 33: 2651-2660 and Litt et al. U.S. Patent 6,635,469 (effective filing date of July 2, 1996).

For present claims 1, 3, 5, 7-8, and 11, Bonafe et al. teach methods of pressure-induced aggregate dissociation and refolding of hemocyanin comprising (a) obtaining a sample comprising protein aggregates (i.e. without denaturing agents; protein folding intermediates), (b) subjecting the sample to high pressure wherein a portion dissociates (i.e. not completely dissociated, dimers present), and (c) returning the sample to ambient pressure wherein a portion refolds (please refer to the entire references particularly the abstract; Results section).

However, Bonafe et al. do not teach inclusion bodies or chaotropic agents.

For present claims 2, 4, 6, 9-10, and 12, Litt et al. teach methods of recovering properly folded proteins from a sample comprising protein aggregates comprising inclusion bodies (please refer to the entire specification particularly column 17, lines 45-67 and column 18, lines 1-31). In addition, Litt et al. specifically teach that chaotropic agents are optional and that non-chaotropic agents may be utilized (please refer to the entire specification particularly column 4, lines 35-49; column 7, lines 27-40; column 8, lines 20-32; column 15, lines 51-67; column 16, lines 1-17; column 17, lines 45-67 and column 18, lines 1-31; column 19, lines 60-67; column 20, lines 1-5).

In addition, the claims would have been obvious because a particular known technique (utilizing chaotropic agents and isolation of proteins from inclusion bodies taught by Litt et al.) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

December 30, 2008